

IN THE CLAIMS

Amendments to the Claims:

Please cancel claims 56, 58, and 59, without prejudice or disclaimer.

Please amend claims 48, 51, and 55 as follows.

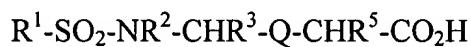
Following amendments, claims 48-55 and 57 will be pending in the application.

The following listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claims 1-47 (Canceled).

Claim 48 (Currently amended): A method of treating inflammatory disorders in a mammalian patient, which disorder involves binding of alpha-9 integrin to an alpha-9 integrin ligand in a mammalian patient, which method comprises administering to a mammalian subject in need thereof an effective dosage of an alpha-9 integrin antagonist compound which compound is represented by the formula:



wherein:

R^1 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclic, substituted heterocyclic, heteroaryl and substituted heteroaryl;

R^2 is selected from the group consisting of hydrogen, alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and R^1 and R^2 together

with the nitrogen atom bound to R² and the SO₂ group bound to R¹ can form a heterocyclic or a substituted heterocyclic group;

R³ is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic, substituted heterocyclic and, when R² does not form a heterocyclic group with R¹, R² and R³ together with the nitrogen atom bound to R² and the carbon atom bound to R³ can form a heterocyclic or a substituted heterocyclic group;

R⁵ is -(CH₂)_x-Ar-R^{5'} where R^{5'} is selected from the group consisting of

-O-Z-NR⁸R^{8'} and -O-Z-R¹² wherein R⁸ and R^{8'} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclic, substituted heterocyclic, and where R⁸ and R^{8'} are joined to form a heterocyclic or substituted heterocycle, R¹² is selected from the group consisting of heterocycle and substituted heterocycle, and Z is selected from the group consisting of -C(O)- and -SO₂-,

Ar is aryl, heteroaryl, substituted aryl or substituted heteroaryl,

X is an integer of from 1 to 4;

Q is -C(X)NR⁷- wherein R⁷ is selected from the group consisting of hydrogen and alkyl; and X is selected from the group consisting of oxygen and sulfur; and

pharmaceutically acceptable salts thereof, wherein said compound has a K_i or IC₅₀ of less than 100 μM, as determined in an assay that measures inhibition of binding between alpha-9 integrin and alpha-9 integrin ligand.

Claim 49 (Previously presented): The method of claim 48, wherein said inflammatory condition is characterized by increased neutrophil activity.

Claim 50 (Previously presented): The method of Claim 49, wherein said alpha-9 integrin antagonist compound is selected from a group of compounds which are both alpha-4 integrin and alpha-9 integrin antagonists.

Claim 51 (Currently amended): ~~The method of Claim 49, wherein said alpha-9 integrin antagonist is A method for treating inflammatory disorders in a mammalian subject, which disorders are characterized by increased neutrophil activity and involve binding of alpha-9 integrin to an alpha-9 integrin ligand, wherein the method comprises administering to the mammalian subject in need thereof an alpha-9 integrin antagonist compound selected from the group consisting of:~~

N-(toluene-4-sulfonyl)-L-prolyl-L-4-(4-methylpiperazin-1-ylcarbonyloxy)phenylalanine,

N-(toluene-4-sulfonyl)-L-prolyl-L-4(N,N-dimethylcarbamoyloxy)phenylalanine,

N-(1-methylpyrazole-4-sulfonyl)-L-prolyl-L-4-(N,N-dimethylcarbamoyloxy)phenylalanine,

N-(toluene-4-sulfonyl)-L-(1,1-dioxo-5,5-dimethyl)thiaprolyl-L-4(N,N-dimethylcarbamoyloxy)phenylalanine,

N-(toluene-4-sulfonyl)-N-methyl-L-alaninyl-L-4-(N,N-dimethylcarbamoyloxy)phenylalanine,

N-(toluene-4-sulfonyl)-L-[(1,1-dioxo)thiamorpholin-3-carbonyl]-L-4-(N,N-dimethylcarbamoyloxy)phenylalanine,

N-(N-p-toluenesulfonyl)prolyl-4-(piperazinoyloxy)phenylalanine,

N-(N-p-toluenesulfonyl)sarcosyl-4-(N,N-dimethylcarbamoyloxy)phenylalanine,

N-(toluene-4-sulfonyl)-L-(5,5-dimethyl)thiaprolyl-L-4-[3-(N,N-dimethyl)propoxy]-phenylalanine, and

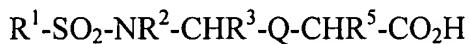
pharmaceutically acceptable salts thereof.

Claim 52 (Previously presented): The method of Claim 48, wherein the alpha-9 integrin ligand is vascular cell adhesion molecule-1 (VCAM-1).

Claim 53 (Previously presented): The method of Claim 48, wherein the alpha-9 integrin antagonist compound inhibits binding between alpha-9 integrin and an alpha-9 integrin ligand, wherein the ligand is selected from the group consisting of osteopontin, tenascin, VCAM-1, and combinations thereof.

Claim 54 (Previously presented): The method of Claim 48, wherein the inflammatory condition is selected from the group consisting of chronic asthma, smooth muscle cell proliferation in atherosclerosis, vascular occlusion following angioplasty, fibrosis and glomerular scarring as a result of renal disease, aortic stenosis, hypertrophy of synovial membranes in rheumatoid arthritis, and inflammation and scarring that occur with the progression of ulcerative colitis, and Crohn's disease.

Claim 55 (Currently amended): A method for inhibiting binding of alpha-9 integrin to an alpha-9 integrin ligand in a mammalian subject, the method comprising administering to a mammalian subject in need thereof a ~~pharmaceutically effective dosage~~ of an alpha-9 integrin antagonist compound, which compound is represented by the formula:



wherein:

R^1 is selected from the group consisting of alkyl, substituted alkyl, aryl, substituted aryl, cycloalkyl, substituted cycloalkyl, heterocyclic, substituted heterocyclic, heteroaryl and substituted heteroaryl;

R^2 is selected from the group consisting of hydrogen, alkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heterocyclic, substituted heterocyclic, substituted alkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, and R^1 and R^2 together with the nitrogen atom bound to R^2 and the SO_2 group bound to R^1 can form a heterocyclic or a substituted heterocyclic group;

R^3 is selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, aryl, substituted aryl, heteroaryl, substituted heteroaryl, heterocyclic,

substituted heterocyclic and, when R² does not form a heterocyclic group with R¹, R² and R³ together with the nitrogen atom bound to R² and the carbon atom bound to R³ can form a heterocyclic or a substituted heterocyclic group;

R⁵ is -(CH₂)_x-Ar-R^{5'} where R^{5'} is selected from the group consisting of -O-Z-NR⁸R^{8'} and -O-Z-R¹² wherein R⁸ and R^{8'} are independently selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, heterocyclic, substituted heterocyclic, and where R⁸ and R^{8'} are joined to form a heterocyclic or substituted heterocycle, R¹² is selected from the group consisting of heterocycle and substituted heterocycle, and Z is selected from the group consisting of -C(O)- and -SO₂-,

Ar is aryl, heteroaryl, substituted aryl or substituted heteroaryl,

X is an integer of from 1 to 4;

Q is -C(X)NR⁷- wherein R⁷ is selected from the group consisting of hydrogen and alkyl; and X is selected from the group consisting of oxygen and sulfur; and

pharmaceutically acceptable salts thereof.

Claim 56 (Canceled).

Claim 57 (Previously presented): The method of Claim 55, wherein said alpha-9 integrin antagonist compound is selected from a group of compounds which are both alpha-4 integrin and alpha-9 integrin antagonists.

Claims 58 and 59 (Canceled).